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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,682	10/16/2001	Barney Scott Graham	VBLT:003US/SLH	6636

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EXAMINER

JIANG, SHAOJIA A

ART UNIT PAPER NUMBER

1617

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/981,682

Applicant(s)

GRAHAM ET AL.

Examiner

Shaojia A Jiang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11 and 13-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11 and 13-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

In view of the appeal brief filed on May 26, 2004, PROSECUTION IS HEREBY REOPENED. A new ground of rejection set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

As recorded in the previous Office Action October 2, 2003, claims 10, 12, and 21-50 are cancelled.

Currently, claims 1-9, 11 and 13-20 are pending in this application.

Election/Restrictions

Applicant's election *without* traverse of the invention of Group I, and the invention of species of respiratory syncytial virus (RSV) as a single virus to be treated, submitted February 3, 2003 has been recorded in the previous Office Action April 9, 2003.

On consideration by the examiner, the specie election requirement is withdrawn.

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The following is the new ground(s) of rejection(s).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-6 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for inhibiting infection of a cell in a patient or a patient having an existing viral infection disclosed in the specification employing the particular HMG-CoA reductase inhibitors herein, does not reasonably provide enablement for inhibiting infection of a cell in a patient who ^{does} ~~doe~~ not have an existing viral infection.

These claims would be reasonably interpreted as drawn to the method of preventing a viral infection in a patient since the patient herein does not have an existing viral infection". Moreover, the limitation "said subject does not have an existing viral infection" in claim 2 is deemed to contradict the subject having a virus in claim 1. Further, if the subject does not have an existing viral infection, the claimed method of inhibiting infection loses its utility or therapeutic purpose, since there is no need to inhibit any viral infection in a subject that does not have an existing viral infection at all.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d

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1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The instant invention pertains to the method of inhibiting infection of a cell in a patient who dose not have an existing viral infection or the method of preventing a viral infection in a patient.

The state of the prior art: The skilled artisan would view that the treatment to prevent a viral infection in a patient totally, absolutely, or permanently, is highly unlikely, not even occurring at the first time; or the skilled artisan would view that inhibiting infection of a cell in a patient who dose not have an existing viral infection totally, absolutely, or permanently, is highly unlikely.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or lack thereof in the art: The skilled artisan would view that the treatment to prevent a viral infection in a patient totally, absolutely, or permanently, is highly unpredictable, not even occurring at the first time; or the skilled artisan would view that inhibiting infection of a cell in a patient who dose not have an existing viral infection totally, absolutely, or permanently is highly unpredictable.

The amount of direction or guidance presented and the presence or absence of working examples: In the instant case, no working examples are presented in the specification as filed showing how to prevent a viral infection in a patient totally, absolutely, or permanently, not even occurring at the first time; or showing how inhibit infection of a cell in a patient who dose not have an existing viral infection totally, absolutely, or permanently. Lack of a working example, however, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

Genentech, 108 F.3d at 1366, states that “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test any HMG-CoA reductase inhibitor compounds encompassed in the instant claims to be administered to a patient to prevent a viral infection in a patient totally, absolutely, or permanently, not even occurring at the first time or to inhibit infection of a cell in a patient who dose not have an existing viral infection totally, absolutely, or permanently, with no assurance of success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a patient" and also recites "said subject" in the same claim. There is insufficient antecedent basis for this limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-9 and 13-16 are rejected under 35 U.S.C. 102(a) as being anticipated by Baldini et al. (*Efficacy and tolerability of pravastatin for the treatment of HIV-1 protease inhibitors-associated hyperlipidemias: a pilot*, PTO-892).

Baldini et al. discloses administering the particular inhibitor of HMG-CoA reductase, pravastatin, to HIV-infected human patients who also administering protease inhibitors included ritonavir plus saquinavir, ritonavir, indinavir, saquinavir, ritonavir plus nelfinavir, and nelfinavir. Thus, the HIV-infected human patients taught by Baldini et al. meet the recitations or limitations of the subject herein, i.e., "said subject is or will become immunosuppressed"; "said subject suffers from severe combined

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immunodeficiency”; “said subject is taking or will take immunosuppressive drugs”; “said subject is or will be a transplant recipient”; “said subject has an existing viral infection” (emphases added). See abstract.

Note that Baldini et al. discloses that the effective amount of pravastatin to be administered is 20 mg/day (see abstract), which are within the effective amounts 10-40 mg/day for pravastatin, indicated in Applicant’s specification (see page 17 line 12 of the specification).

Therefore, Baldini’s method inherently inhibits infection of a cell by a virus in a subject, as claimed herein, since Baldini’s method steps are same as the instant method steps, administering the same compound in the same amount to the same patient population. See *Ex parte Novitski*, 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Note that even the claiming of a new use, new function or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it related to the claimed invention herein.

Thus, Baldini et al. anticipates Claims 1-9 and 13-16.

Claims 1-9 and 13 are rejected under 35 U.S.C. 102(a) as being anticipated by Aboulafia et al. (*Simvastatin-induced rhabdomyolysis in an HIV-infected patient with coronary artery disease*, PTO-892).

Aboulafia et al. discloses administering the particular inhibitor of HMG-CoA reductase, simvastatin, to HIV-infected human. Thus, the HIV-infected human patients taught by Aboulafia et al. meet the recitations or limitations of the subject herein, i.e., "said subject is or will become immunosuppressed"; "said subject suffers from severe combined immunodeficiency"; "said subject is taking or will take immunosuppressive drugs"; "said subject is or will be a transplant recipient"; "said subject has an existing viral infection" (emphases added). See abstract.

Therefore, Aboulafia's method inherently inhibits infection of a cell by a virus in a subject, as claimed herein, since Aboulafia's method steps are same as the instant method steps, administering the same compound to the same patient population. See *Ex parte Novitski*, 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Note that even the claiming of a new use, new function or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it related to the claimed invention herein.

Thus, Aboulafia et al. anticipates Claims 1-9 and 13.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1-9 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Murillas et al. (*Atorvastatin: therapeutic use. Hyperlipidaemia In patients with HIV-1 infection receiving protease inhibitors*, PTO-892).

Murillas et al. discloses administering the particular inhibitor of HMG-CoA reductase, atorvastatin, to HIV-infected human patients who also receiving protease inhibitors. Thus, the HIV-infected human patients taught by Baldini et al. meet the recitations or limitations of the subject herein, i.e., "said subject is or will become immunosuppressed"; "said subject suffers from severe combined immunodeficiency"; "said subject is taking or will take immunosuppressive drugs"; "said subject is or will be a transplant recipient"; "said subject has an existing viral infection" (emphases added). See abstract.

Therefore, Murillas's method inherently inhibits infection of a cell by a virus in a subject, as claimed herein, since Murillas's method steps are same as the instant method steps, administering the same compound to the same patient population. See *Ex parte Novitski*, 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Note that even the claiming of a new use, new function or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it related to the claimed invention herein.

Thus, Murillas et al. anticipates Claims 1-9 and 13-16.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maziere et al. (C24, PTO-1229 submitted June 11, 2002) and Murillas et al. or Baldini et al. in view of Graham et al. (WO 99/62932, PTO-892) and Mills (PTO-892).

Maziere et al. teaches that HMG-CoA reductase inhibitors, such as lovastatin, are useful in a method of inhibiting HIV infective cycle in AIDS patients since lovastatin inhibits HIV-1 expression in H9 human T lymphocytes or viral multiplication. See in Maziere et al., the title, "Summary", and page 66 "Conclusion". Maziere et al. also teaches that the particular nucleoside analog, AZT, is known to be useful in treating viral infection by inhibiting viral replication in humans. See "Introduction" page 63 the left column.

The same disclosure of ~~or~~ Murillas et al. or Baldini et al. has been discussed in the 102(b) rejection set forth above (supra).

The Maziere et al., Murillas et al. and Baldini et al. do not expressly disclose the employment of HMG-CoA reductase inhibitors in a method of inhibiting infection of a cell by a virus which is respiratory syncytial virus (RSV) in a human, a non-human mammal, or a livestock animal. The above cited prior art does also not expressly disclose the

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employment of HMG-CoA reductase inhibitor in combination with ribavarin in a method inhibiting infection of a cell by a virus in a subject.

Graham et al. (WO 99/62932) teaches that the enveloped viruses including RSV and HIV share a common cellular entry mechanism-fusion of the viral envelop; the cell membrane-the RhoA peptides inhibit viral entry for other viruses which are demonstrated to share the cellular entry mechanism common to RSV and HIV (see page 5 lines 5-15).

Mills teaches that ribavarin is a known licensed antiviral agent or drug for RSV infections. The combination of ribavarin and other antiviral agents are also known in the art. See page 39-41.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a HMG-CoA reductase inhibitor in a method of inhibiting infection of a cell by a virus such as RSV in a human, a non-human mammal, or a livestock animal, and to employ a HMG-CoA reductase inhibitor in combination with ribavarin in a method of inhibiting infection of a cell by a virus.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ a HMG-CoA reductase inhibitor in a method of inhibiting infection of a cell by a virus such as RSV in a human, a non-human mammal, or a livestock animal, since a HMG-CoA reductase inhibitor such as lovastatin is known to be useful in a method for inhibiting infection of a cell by a virus, i.e., inhibiting HIV infective cycle in AIDS patients, by inhibiting HIV-1 expression in H9 human T lymphocytes or viral multiplication according to Maziere et al. Moreover, HMG-CoA

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reductase inhibitors in combination with other antiviral agents such as protease inhibitors to be administered to HIV-infected human patients are known in the art according to Murillas et al. or Baldini et al.

Further, both RSV and HIV are the enveloped viruses and share a common cellular entry mechanism-fusion of the viral envelop, according to Graham et al. Thus,, one of ordinary skill in the art would have reasonably expected that lovastatin would also be able to inhibit RSV infective cycle and multiplication as it inhibits HIV infective cycle and multiplication, since both RSV and HIV are the enveloped viruses and share a common cellular entry mechanism-fusion of the viral envelop.

Therefore, one of ordinary skill in the art would have reasonably expected that a HMG-CoA reductase inhibitor would have a beneficial therapeutic effect in inhibiting infection of a cell by a virus such as RSV in a human, a non-human mammal, or a livestock animal.

Additionally, one having ordinary skill in the art at the time the invention was made would have been motivated to add ribavarin in a method of inhibiting infection of a cell by a virus such as RSV, since ribavarin is known to be useful in treating viral infection including RSV by inhibiting viral replication in humans, and combination therapy for treating viral infections is well known in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

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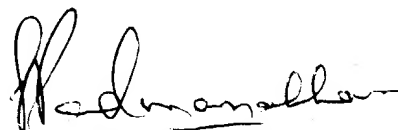
In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner, AU 1617
August 20, 2004



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